Molecular Imaging Guided Therapy: The Perfect Storm

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Clinical Service

Department of Radiology & Imaging Sciences

Culture of Service Excellence

Session I of the Service Excellence Institute (SEI) is winding down as we gear up for Session II. During this time between the sessions, we hope each of us is putting to use the tools acquired in Session I, to become positive change agents, to influence our work environment for our peers, and to deliver individualized experiences for our patients and families. When you return for the second session, we will be building on these tools and learning more service excellence concepts.

Read more in the March Rad Report.

Recent Accomplishments

ACR Outstanding Teacher Award

Dr. Tigges was recognized as an Outstanding Teacher by the American Alliance of Academic Chief Residents in Radiology (A3CR2). The purpose of the award is to recognize an outstanding teacher in...
Clinical Divisions - Nuclear Medicine & Molecular Imaging

The faculty of the Emory Division of Nuclear Medicine & Molecular Imaging offers the highest quality patient care, incorporating the latest knowledge, innovation and equipment. Nuclear Medicine not only uses the most advanced methods, but also helps set the bar for the field. All of the physicians are board certified in nuclear medicine, and some are double-boarded in other fields, particularly Radiology; many have national and international reputations in their fields.

Equipment includes PET/CT and SPECT/CT scanners at Emory University Hospital (Clifton campus), and Emory University Hospital Midtown. We offer a wide variety of specialized nuclear medicine therapies including that for thyroid cancer, bone cancer pain palliation, lymphoma, neuroendocrine tumors and Y-90 liver therapy in cooperation with Interventional Radiology. Research devices at our disposal include one of the few PET-MR units in the world, a high-resolution brain PET scanner, micro-PET for animal research, and a research cyclotron. A full range of nuclear medicine and PET/CT services are also provided at Grady Memorial Hospital and the Atlanta VA Medical Center. The Division is integrally involved in research conducted by the Emory University School of Medicine faculty, including close collaboration with colleagues in radiology and cardiology and at the Emory Winship Cancer Institute. Our faculty are principal investigators and co-investigators on many research grants including those sponsored by the NIH.

- David M. Schuster, MD
  Director, Division of Nuclear Medicine and Molecular Imaging

Recent Accomplishments
Let’s start with a case...

- 74 year old female with chronic diarrhea
- Enlarged porta-hepatic nodes
  - Biopsy positive for NET
- Chromogranin A is 6336
- Multiple staging studies performed but we will review two that provide molecular interrogation of the tumor process.
  - $^{111}$Indium Octreoscan
  - $^{18}$F-FDG PET
$^{111}$Indium OctreoScan

$^{111}$In-octreotide is a conjugate of 8 of the amino acids from somatostatin. Highest affinity for subtype 2. Labeled with Indium-111.

Intensely somatostatin receptor avid lesions.
And there is little uptake on $^{18}$F-FDG PET…
What have we learned?

- Staging: Confident that this is the only site of disease

- Since Octreoscan has highest uptake in well differentiated tumors
  - And FDG typically has higher uptake in poorly differentiated tumors

- Then we are confident that the lesion is well differentiated and...
What have we learned?

- This inoperable patient will likely benefit from Sandostatin therapy
- Prognostic information: Higher survival with lower FDG uptake.
- Of course, biopsy is key
- Imaging can be used to interrogate globally
  - Biopsy subject to sampling error
  - Cannot biopsy all lesions
Is it possible to close the loop to also include specific guidance of a therapy and even the therapy itself?
Molecular Medicine

- In fact we have been using targeted molecular techniques for years in this manner.
- One example is radio-iodine scanning and therapy for thyroid carcinoma.
Thyroid Carcinoma

- After thyroid surgery, we use the radio-iodine scan to localize how much thyroid tissue remains and if there are metastases
- Modify therapy dose accordingly
- Use radio-iodine to also ablate and treat
- Then take advantage of that therapeutic dose for an extremely sensitive post-therapy ultra-diagnostic study
Pushing the Envelope

- Can we extend these concepts further by collaborating with other disciplines and subdisciplines?
- The answer is a resounding: YES!
- We not only can, but we must work in teams to advance all our areas of expertise.
Let’s look at another patient...

- 77 year old female with metastatic NET
  - Presented with progressive liver predominant disease

- Symptoms controlled on Sandostatin
  - Outside planar OctreoScan positive
  - $^{90}$Y microspheres therapy scheduled by IR
**90Y Microsphere Brachytherapy**

- Glass or resin beads introduced through the hepatic artery into liver
- Delivers tumoricidal doses while sparing normal liver tissue supplied by portal circulation
- 90Y has a half-life of 64.2 hours and undergoes beta decay
- Average penetration 2.5 mm

*Adapted courtesy of Bree Eaton, MD*
# 90Y Microspheres for Therapy

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Glass (TheraSphere)</th>
<th>Resin (SirSpheres)</th>
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<tr>
<td>Size</td>
<td>20-30 μm</td>
<td>20-60 μm</td>
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<tr>
<td>Isotope</td>
<td>Yttrium-90 in glass matrix</td>
<td>Yttrium-90 on resin surface</td>
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<tr>
<td>Specific Gravity</td>
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<td>Low</td>
</tr>
<tr>
<td>Activity/sphere (at calibration)</td>
<td>2500 Bq</td>
<td>50 Bq</td>
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<tr>
<td># of dose sizes</td>
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<td>1</td>
</tr>
<tr>
<td></td>
<td>(3,5,7,10,15,20 GBq)</td>
<td>(3 GBq)</td>
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<tr>
<td># spheres/dose</td>
<td>1.2-8 Million</td>
<td>40-80 Million</td>
</tr>
<tr>
<td># spheres/3GBq dose</td>
<td>1.2 Million</td>
<td>40-80 Million</td>
</tr>
<tr>
<td>US – FDA Approval</td>
<td>HCC</td>
<td>CRC metastases with FUDR pump</td>
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Dose Planning and Mapping

- $^{99m}$Tc MAA to show where the dose will go since MAA is similar size range to the microspheres
- We also use molecular imaging to help plan the dose
Dose distribution from MAA study
Also lung shunt to for dose to lung

Extrahepatic (duodenal) uptake noted and
will be avoided during therapy.
Liver and Tumor Volumes from the OctreoScan on Advanced Workstation
Therapy and Post-Therapy Imaging

• Patient treated in 2 sessions to preserve liver function after each therapy
  – Usual in US
  – Europe more often do whole liver

• Make use of Bremsstrahlung effect to image post therapy
  – German for Braking Radiation
  – Low energy x-rays

Bremsstrahlung

\[ \beta^+ \]
Bremsstrahlung imaging to prove entire liver treated and no extrahepatic deposition

Right lobe therapy  Left lobe therapy  Fusion to complete the puzzle
Example: Fusion

Fused FDG PET and Bremsstrahlung confirms $^{90}\text{Y}$ coverage of tumor
Another case where Bremsstrahlung demonstrated how much tumor was treated and that additional therapy needed.

Detail from OctreoScan

Post-left lobe Bremsstrahlung

Fusion shows portion of tumor (white) untreated in this session (black). (Unavoidable 2° vascular anatomy)
Cutting Edge: Working with colleagues in Radiation Oncology to calculate Absorbed Dose and correlate with response

Pre-treatment PET

Post-treatment PET

Adapted courtesy of Bree Eaton, MD
Cutting Edge: Do we modify dose for differences in anatomic tumor versus functional tumor?
Molecular Image Guidance

- Molecular Imaging for Staging and Prognosis
- General Guidance Type of Therapy
- Follow-up and Restaging
- Specific Guidance of Therapy Itself
Getting back to our patient. Hepatic disease stabilized but a year later breakthrough symptoms. Is the tumor now dedifferentiating?

Lack of uptake on $^{18}$F-FDG PET suggests it is not...
Return to Functional Neuroendocrine Imaging

- OctreoScan shows significant extrahepatic disease so tumor still fairly well differentiated
- We will do a related diagnostic scan:
  - $^{123}$I MIBG
    - Metaiodobenzylguanidine
    - Norepinephrine analog
- If there is uptake in metastasis can then offer therapy with the beta emitter $^{131}$I MIBG
$^{123}$I MIBG

Uptake in liver but also mesenteric and retroperitoneal nodes and other distant disease
**131I MIBG Therapy**

- We saw her in consult
  - Candidate for high dose 131I MIBG therapy
- Not a cure but multiple studies show efficacy
    - >50% improved symptoms with increased survival
  - *Postema et al.* Cancer Biotherapy & Radiopharm 2009;24:519
    - Symptomatic relief in the vast majority of patients treated
    - Biochemical responses in about half
    - Radiographic responses in roughly one third
- Will get post-therapy scan to ensure metastases targeted by therapy and then follow-up using anatomic and molecular imaging
Molecular Medicine

Molecular Techniques become the Therapy

Molecular Imaging for Staging, Prognosis, Follow-up

Specific Guidance of Therapy

General Guidance Type of Therapy
The Perfect Storm of Theranostics

- Molecular Imaging for Staging, Prognosis, Follow-up
- General Guidance Type of Therapy
- Specific Guidance of Therapy
- Molecular Techniques become the Therapy
Theranostics is Now

• *Lee et al. AJR 2011;197:318*
  – System that integrates a diagnostic test with a therapeutic intervention targeting a molecular feature of disease
  – May be as traditional as radio-iodine therapy of thyroid cancer
  – Or utilizing molecular techniques to guide type and design of therapy
Future Theranostics

- Or cutting edge such as $^{18}$F-Estradiol PET to predict response to tamoxifen or $^{18}$F-FMISO PET to direct radiation boost to hypoxia
- Nanoparticles with targeted probes for PET and/or MR that can deliver radionuclide or drug therapy – With possible image guided energy activation
- Customized agents with characteristics of the individual tumor to direct therapy not only anatomically but also biologically
Molecular Imaging

- Molecular imaging is the visualization, characterization, and measurement of biological processes at the molecular and cellular levels
  - Includes radiotracer imaging/nuclear medicine, MR imaging, MR spectroscopy, optical imaging, ultrasound, and others
Molecular Imaging

- Wealth of added value that nuclear medicine and molecular imaging can bring to interventions
- May use a radiotracer for its physical, biologic, and/or therapeutic characteristics
- Other theranostic techniques such as nanoparticles show great promise
Likely a new type of medical professional with specialized training will ideally be required as we move forward in teams.